REMARKS

(A) STATUS OF THE APPLICATION

Applicants thank the Examiner for her explanation of the rejections in the Final Office Action dated September 29, 2006.

(I) DISPOSITION OF CLAIMS

(i) Claims 1-31 are pending in the application.

(ii) Claims 1-19 are withdrawn from consideration under 37 C.F.R. § 1.142(b).

(iii) Claim 20 is objected to.

(iv) Claims 20-28, and 30-31 are rejected under 35 U.S.C. § 102(e).

(v) Claims 20-31 are rejected under 35 U.S.C. § 102(b).

(vi) Claims 20-31 are rejected under 35 U.S.C. § 102(a)/(b).

(II) APPLICANTS' ACTION

(i) Applicants have amended Claims 20, 25, 26, and 30. Support for the amendments are the original claims. No new matter was added.

(ii) Applicants also respond to the above rejections.

(B) RESPONSE TO OBJECTION TO CLAIM 20

Claim 20 is objected to because it contains an extraneous sequence of words after the period ending the previously examined claim. In response, Applicants have deleted said "extraneous sequence of words."

In the ensuing discussion, comments under the sub-heading "Examiner's Comments" are attributed to the Examiner. Unless specified, Applicants do not generally agree with the assertions made by the Examiner under that sub-heading. Applicants give their views in the comments under the sub-heading "Applicants' Response."

(C) RESPONSE TO REJECTION UNDER 35 U.S.C. § 102(E)
U.S. PATENT NO. 6,361,944 TO MIRKIN, *ET AL.*—CLAIMS 20-28 & 30-31

(I) Examiner's Comments

The Examiner has rejected Claims 20-28, and 30-31 under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 6,361,944 to Mirkin, *et al.* (*hereinafter*, "Mirkin").

Particularly, Mirkin discloses a geometric nanostructure comprising at least two (as it relates to Claim 30) and at least three (as it relates to Claim 20) complexes in a spatially arranged and ordered pattern, the complexes comprising a nanoparticle and a **"single ligand (i.e. a single type ligand/particle, [shown in] Fig. 25)**, wherein the ligand has a proximal portion attached to the nanoparticle. . .and a distal portion wherein the complexes are each affixed to each other through the distal portion."[1]

Mirkin anticipates dependent Claims 21-28, and 31 because it also discloses the narrowing limitations of said claims.[2]

(II) Applicants' Response

Applicants disagree with the Examiner's interpretation of Mirkin.

Applicants' invention relates to a single ligand, i.e., a single unit as distinguished from a single-type of a ligand being affixed on a nanoparticle. Mirkin, on the other hand, teaches nanoparticles comprising **multiple ligands on each nanoparticle** (see Col. 18, Lines 1-5). Mirkin does not teach any method for isolating nanoparticles having a single ligand attached thereto. Applicants submit that this is only taught in the present application and forms one of the bases of the invention.

In fact, Applicants amended the claims in Response to the Office Action dated April 12, 2006 (*hereinafter*, the "April Office Action") reciting the limitation that each nanoparticle

[1] See Final Office Rejection dated September 29, 2006, Page 3, Paragraph No. 4. (Emphasis added)..
[2] *Id.* at Pages 3-4.

comprises a single ligand, i.e., a single unit of a ligand (which should not be confused with a "single-type" of a ligand of Fig. 25, cited by the Examiner).

However, the Examiner did not find Applicants' arguments in the April Office Action Response persuasive. Applicants quote the Examiner's comments from the present Office Action below:

> Applicant [*sic*] further asserts that Mirkin only teaches multiple ligands on each particle and does not teach methods for isolating particles having a single ligand attached. The argument has been considered but is not found persuasive because the claims require a "single ligand". Mirkin teaches a single ligand (e.g. ligand "c" as illustrated in Fig. 25B). Hence, Mirkin specifically teaches a single type of ligand attached to the particle. Applicant [*sic*] appears to be asserting that the claims are limited to a single molecule of a single ligand. However, the claims are not so limited. The instant claims define a particle as "comprising" a single ligand. The open claim language "comprising" encompasses additional elements and/or copies of the single ligand. Therefore Mirkin anticipates the structure as claimed. (Emphasis added).

In other words, the Examiner is not persuaded because the transitional phrase "comprising" used in Claims 20 and 30 can possibly include more than one unit of a single ligand, which would then encompass claim scope disclosed in Mirkin.

As a corollary to the Examiner's conclusion, Applicants assume that the Examiner **would be persuaded** that Mirkin does not anticipate Claims 20 and 30 (and their dependent claims) if Applicants were to devise Claims 20 and 30 in such manner that said claims clearly indicate that **only one unit** of a ligand is affixed to a nanoparticle.

Thus, if Claims 20 and 30 were amended to replace the transitional phrase "comprising" with the transitional phrase "consisting of," it would limit the claims' scope to a single unit of ligand on a nanoparticle and would be sufficiently persuasive an argument for the Examiner to withdraw the anticipation rejection.

However, Applicants have decided not to change the transitional phrase. Applicants submit that if said change was instituted, in addition to attending to the Examiner's rejection, it would create an argument that Applicants (inadvertently or otherwise) surrendered claim scope beyond the "single unit of ligand," provided by Claims 20 and

30. For example, a nanoparticle-ligand complex consisting of (a) a nanoparticle and (b) a single ligand would preclude inclusion in such complex of anything but the two items. Therefore, Applicants expressly refrain from making such a replacement.

The real issue is to convey in the claims that only one unit of a ligand is present on a nanoparticle, and that more than one units are not present. Applicants have therefore amended Claims 20 and 30 to include a proviso that "said single ligand is the only ligand unit affixed to the surface of said nanoparticle."

Applicants respectfully submit that because Claims 20-28, and 31 depend on Claims 20 and 30, and because Claims 20 and 30, the independent claims are not anticipated, and that the dependent claims with narrowing limitations are also not anticipated.

(D) RESPONSE TO REJECTION UNDER 35 U.S.C. § 102(B)
U.S. PATENT NO. 6,261,779 TO BARBERA-GUILLEM, *ET AL.*—CLAIMS 20-31

(I) Examiner's Comments

The Examiner has rejected Claims 20-31 under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 6,261,779 to Barbera-Guillem, *et al.* (*hereinafter,* "Guillem").

Particularly, Guillem discloses a geometric nanostructure comprising at least three complexes in a spatially arranged and ordered pattern, "the complexes comprising a nanoparticle. . .and a **single ligand (multiple copies of the same ligand, e.g., Fig. 3),** wherein the ligand has a proximal portion attached to the nanoparticle. . . and a distal portion wherein the complexes are each affixed to each other through the distal portion."[3]

Guillem anticipates dependent Claims 21-29, and 31 because it also discloses the narrowing limitations of said claims.[4]

[3] See Final Office Rejection dated September 29, 2006, Page 5, Paragraph No. 6.(Emphasis added).
[4] *Id.* at Pages 6-7.

(II) Applicants' Response

Applicants disagree with the Examiner's interpretation of Guillem.

Applicants' invention relates to a single ligand, i.e., a single unit as distinguished from a single-type of a ligand being affixed on a nanoparticle. Guillem, on the other hand, teaches nanoparticles comprising **multiple ligands on each nanoparticle** (see e.g., Fig. 3). Guillem teaches the formation of nanocrystals comprising oligonucleotide ligands for use in the amplification of a signal in a bioassay. The object of Guillem is that nanoparticles comprising a plurality of oligos will be aggregated into dendrimers in the presence of a target nucleic acid that has the ability to hybridize to the oligos. The increased mass of the dendrimer enhances the signal for detection of the target nucleic acid.

However, regarding Guillem, the Examiner did not find Applicants' arguments in the April Office Action Response persuasive for the same reason that she did not find persuasive Applicants' arguments regarding Mirkin.

It is the Examiner's view that Guillem describes a geometric nanostructure as described in the abstract, and that all other limitations of the claims are further described. However, Guillem does not teach any method for isolating nanoparticles having a single ligand attached thereto. Applicants submit that this is only taught in the present application and forms one of the bases of the invention.

It is an object of the invention of Guillem to provide a plurality of ligands on each nanoparticle (see the abstract; Col. 8, Line 61 – Col. 9, Line 10). This is in concert with the Guillem invention, that being a method to aggregate nanoparticles to enhance the signal associated with the presence of target DNA. As with Mirkin, Guillem does not need, and does not teach, a method for isolating nanoparticles associated with a single ligand (by "single ligand" here is meant a single unit of a ligand on a nanoparticle and not multiple units of a single-type of ligand on the nanoparticle).

Applicants incorporate the arguments from the previous section in regards to replacement of the transitional phrase "comprising" with the transitional phrase "consisting of" and other arguments relating to the "single ligand."

Applicants respectfully submit that because Claims 20-29, and 31 depend on Claims 20 and 30, and because Claims 20 and 30, the independent claims, are not anticipated, the dependent claims with narrowing limitations are also not anticipated.

(E) RESPONSE TO REJECTION UNDER 35 U.S.C. § 102(A)/(B) THE NIEMEYER, *ET AL.* PAPER IN CHEMBIOCHEM—CLAIMS 20-31

(I) Examiner's Comments

The Examiner has rejected Claims 20-31 under 35 U.S.C. § 102(a)/(b) as anticipated by the journal article of Niemeyer, *et al.* (*hereinafter,* "Niemeyer").[5]

Particularly, Niemeyer discloses a geometric nanostructure comprising at least two (as it relates to Claim 30) and at least three (as it relates to Claim 20) complexes in a spatially arranged and ordered pattern, "the complexes comprising a nanoparticle. . . and a single ligand (DNA:STV [ratio at] 3:2, providing at least some STV with a single copy of a single ligand. . .), wherein the ligand has a proximal portion attached to the nanoparticle and a distal portion wherein the complexes are each affixed to each other through the distal portion."[6]

Niemeyer anticipates dependent Claims 21-28, and 31 because it also discloses the narrowing limitations of said claims.[7]

(II) Applicants' Response

[5] Niemeyer, C. M., *et al.*, "Nucleic Acid Supercoiling as a Means for Ionic Switching of DNA—Nanoparticle Networks," *Chembiochem*, 2001, 2, 26-264.
[6] See Final Office Rejection dated September 29, 2006, Page 7-8, Paragraph No. 9.
[7] *Id.* Pages 3-4.

Applicants disagree with the Examiner's interpretation of Niemeyer.

Niemeyer relates to DNA-"Nanoparticle" networks, wherein the "nanoparticle" is a Streptavidin particle (see for example, *Abstract*). Streptavidin (STV) is a protein. Streptavidin is not a metal. Niemeyer just happens to call it a "nanoparticle." Niemeyer further discusses its "DNA-Nanoparticle" system:

> Within the context of basic studies on DNA-linked nanoparticle networks, the oligomeric aggregates generated from bioorganic STV particles and bis-biotinylated dsDNA are suitable model systems to gain insight into the properties of complex particle networks. The STV functions as a 5 nm model particle which can realize only a limited variation in its connectivity to other particles within the network.

On the other hand, Applicants' invention relates to nanoparticles that are necessarily metallic (See definition of "Nanoparticles" in Specification, on Page 4, Lines 34-36).[8] Clearly, Niemeyer cannot anticipate the present invention because it uses Streptavidin, a non-metallic, bio-organic material.

Furthermore, STV protein is a tetramer having a total of four binding sites that can accommodate four DNA ligands. Niemeyer claims that experimental observation showed two-three bindings.[9] As discussed previously, Applicants' invention relates to a single unit of a ligand affixed on a nanoparticle. Finally, Niemeyer's product is a population of clusters with protein (particle) number ranging from two and higher. It does not demonstrate a control of the nanostructure. On the other hand, in the present invention, the complex relates to a homogeneous population of one type of cluster.

Applicants respectfully submit that because Claims 20-29, and 31 depend on Claims 20 and 30, and because Claims 20 and 30, the independent claims, are not anticipated, the dependent claims with narrowing limitations are also not anticipated.

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[8] From Specification, Page 4, Lines 34-36:

> "Nanoparticles" are herein defined as metallic particles with an average particle diameter of between 1 and 100 nm. Preferably, the average particle diameter of the particles is between about 1 and 40 nm.

[9] See Niemeyer, Page 260, Col. 1, Line 6-8 from the bottom.

CONCLUSION

In view of the above remarks, Applicants respectfully submit that the stated grounds of rejection have been properly traversed, accommodated, or rendered moot and that a complete response has been made to the Final Office Action mailed on September 29, 2006.

Therefore, Applicants believe that the application stands in condition for allowance with withdrawal of all grounds of rejection. A Notice of Allowance is respectfully solicited. If the Examiner has questions regarding the application or the contents of this response, the Examiner is invited to contact the undersigned at the number provided.

Applicants believe that a that a one-month extension of time is required under 37 C.F.R. § 1.136(a). Should there be a fee due which is not accounted for, please charge such fee to Deposit Account No. 04-1928 (E. I. du Pont de Nemours & Co.).

Respectfully Submitted,

BY:

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